

CLAIMS:

1. An adjuvant composition comprising a Th1-activating alkaloid.
- 5 2. The composition of claim 1 further comprising an auxiliary adjuvant, for example an auxiliary adjuvant selected from:
  - (a) a type 2 adjuvant (e.g. alum and/or MF59); and/or
  - (b) a type 1 adjuvant; and/or
  - (c) a balanced adjuvant.
- 10 3. The composition of claim 2 wherein the auxiliary adjuvant comprises alum.
4. The composition of claim 3 wherein the alum comprises an aluminium salt, for example selected from aluminium hydroxide, aluminium phosphate or a mixture of aluminium hydroxide and aluminium phosphate.
- 15 5. The composition of claim 3 or claim 4, wherein the composition consists essentially of the Th1-activating alkaloid and alum.
6. The composition of any one of claims 2 to 4 wherein the auxiliary adjuvant is selected from:
  - 20 (a) a cytokine;
  - (b) a depot-forming agent;
  - (c) a saponin;
  - (d) a submicron oil-in-water emulsion;
  - (e) a CpG;
  - 25 (f) a lipid A derivative;
  - (g) an MDP;
  - (h) an ISCOM®;
  - (i) an antigen-presenting cell (APC) (for example, a dendritic cell);
  - (j) a cytotoxic T lymphocyte (CTL);
  - 30 (k) a synergistic combination of any of the above.
7. The composition of any one of the preceding claims, for use in therapy or prophylaxis.
8. The composition of claim 7, for use in immunotherapy or immunoprophylaxis.
- 35 9. The composition of claim 8, for use in vaccination.
10. Use of the composition of any one of the preceding claims for the manufacture of a vaccine for use in therapy or prophylaxis.
- 40 11. Use of claim 10 wherein the therapy or prophylaxis is immunotherapy or immunoprophylaxis.
12. Use of claim 11 wherein the immunotherapy or immunoprophylaxis comprises vaccination.

13. A vaccine comprising the composition of any one of claims 1 to 9 and one or more antigen(s).
14. The vaccine of claim 13 which is a subunit vaccine.
- 5 15. The vaccine of claim 13 or claim 14 which is a conjugate vaccine.
16. The vaccine of claim 13 which is a DNA vaccine.
- 10 17. The vaccine of any one of claims 13 to 16 which is a recombinant vaccine.
18. The vaccine of any one of claims 13 to 17 which is a mucosal vaccine.
19. The vaccine of any one of claims 13 to 18 which is a therapeutic vaccine.
- 15 20. The vaccine of any one of claims 13 to 18 which is a prophylactic vaccine.
21. The vaccine of any one of claims 13 to 20 wherein the antigen(s) comprise one or more:
- 20 (a) nucleic acid(s) which encode one or more antigenic protein(s);
- (b) protein(s) or peptide(s);
- (c) glycoprotein(s);
- (d) polysaccharide(s) (e.g. carbohydrate(s));
- (e) fusion protein(s);
- (f) lipid(s);
- 25 (g) glycolipid(s);
- (h) peptide mimic(s) of polysaccharides;
- (i) carbohydrate(s) and a protein(s) in admixture;
- (j) carbohydrate-protein conjugate(s);
- (k) cells or extracts thereof;
- 30 (l) dead or attenuated cells, or extracts thereof;
- (m) tumour cells or extracts thereof;
- (n) viral particles (e.g. attenuated viral particles or viral components);
- (o) allergen(s);
- (p) mixtures of any of (a) to (o).
- 35 22. The vaccine of any one of claims 13 to 21 wherein the antigen comprises a bacterial antigen.
23. The vaccine of any one of claims 13 to 21 wherein the antigen comprises a viral antigen.
24. The vaccine of any one of claims 13 to 21 wherein the antigen comprises a fungal antigen.
- 40 25. The vaccine of any one of claims 13 to 21 wherein the antigen comprises a protozoal antigen.

26. The vaccine of any one of claims 13 to 21 wherein the antigen comprises a prion antigen.

27. The vaccine of any one of claims 13 to 21 wherein the antigen comprises a neoantigen or tumour-associated antigen.

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28. The vaccine of any one of claims 13 to 21 wherein the antigen comprises a self-antigen.

29. The vaccine of any one of claims 13 to 28 wherein the antigen is dose-spared.

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30. The vaccine of any one of claims 13 to 29 wherein the alkaloid is present in an amount sufficient to activate a Th1 response to the antigen(s).

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31. A method for inducing or enhancing immunogenicity of an antigen in a subject to be treated, comprising administering to said subject the vaccine of any one of claims 13 to 30 in an amount effective to induce or enhance the immunogenicity of the antigen in the subject.

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32. A method for eliciting a type 1 immune response to an antigen in a subject to be treated, comprising administering to said subject the vaccine of any one of claims 13 to 31 in an amount effective to elicit a type 1 immune response to the antigen in the subject.

33. A method for polarizing an immune response to an antigen in a subject to be treated from type 2 towards type 1, comprising administering to said subject the vaccine of any one of claims 13 to 32 in an amount effective to polarize the immune response to the antigen from Th2 towards Th1.

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34. A method for augmenting a type 2 immune response to an antigen in a subject to be treated with a type 1 immune response, comprising administering to said subject the vaccine of any one of claims 13 to 33 in an amount effective to augment the type 2 response to the antigen with a type 1 response.

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35. The method of any one of claims 33 to 34 wherein the vaccine is administered orally, mucosally, topically, epicutaneously, intramuscularly, intradermally, subcutaneously, intranasally, intravaginally, sublingually or *via* inhalation.

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36. Use of the composition of any one of claims 1 to 9 for the manufacture of a vaccine (for example a vaccine as defined in any one of claims 13 to 30) for use in therapy or prophylaxis (for example in a method as defined in any one of claims 31 to 35).

37. The invention of any one of the preceding claims wherein the Th-1 activating alkaloid is selected from the following classes:

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- (g) piperidines alkaloids;
- (h) pyrroline alkaloids;
- (i) pyrrolidines alkaloids;
- (j) pyrrolizidine alkaloids;
- (k) indolizidine alkaloids;

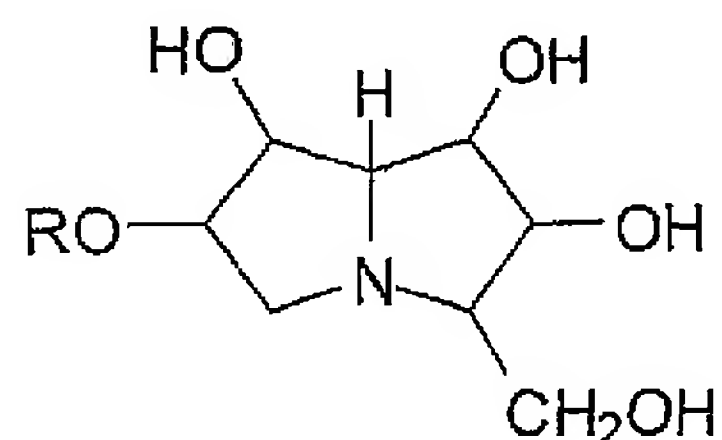
(l) nortropanes alkaloids.

38. The invention of any one of the preceding claims wherein the Th-1 activating alkaloid is polyhydroxylated.

5 39. The invention of any one of the preceding claims wherein the Th-1 activating alkaloid has a molecular weight of 100 to 400 Daltons (for example 150 to 300 Daltons, e.g. 200 to 250 Daltons).

40. The invention of any one of the preceding claims wherein the Th-1 activating alkaloid is polar or non-polar.

10 41. The invention of any one of the preceding claims wherein the Th-1 activating alkaloid has the formula:



15 wherein R is selected from the group comprising hydrogen, straight or branched, unsubstituted or substituted, saturated or unsaturated acyl, alkyl (e.g. cycloalkyl), alkenyl, alkynyl and aryl groups, or a pharmaceutically acceptable salt or derivative thereof.

42. The invention of claim 41 wherein the Th-1 activating alkaloid is 3,7-di*epi*casuarine having the formula:

